REMARKS

Applicants submit this response to the Office Action dated October 6, 2006. Claims 4-23 were withdrawn from consideration as being drawn to a non-elected invention. Claims 1-3 are pending, and applicants elected SEQ ID NOs:26, 28, 33, 37, 41, 45, 62, and 64.

Title. The Examiner stated that the title is not descriptive. The Title as amended herein addresses this issue, and applicants respectfully request withdrawal of this ground for objection.

Priority. The Examiner stated that the filing date of the claims is deemed to be the filing date of provisional application 60/428,130, filed November 21, 2002, because the provisional application 60/331,958, filed November 21, 2001, allegedly fails to provide adequate support for claim 1-3.

35 U.S.C. §112, first paragraph. Claim 3 is rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly is not enabling for any isolated antibody comprising one of the sequences recited in claim 3. The Examiner did state that the specification is enabling for an isolated antibody comprising one specific V_H comprising three CDRs and one specific V_L comprising three CDRs. The Examiner cited Paul, Fundamental Immunology, pages 37, 43, 58 and 59 (1999) for the statement that an intact antigen-binding site requires the association of the complete heavy and light chain variable regions, each of which consists of three CDRs. The Examiner also cited Rudikoff *et al.*, Proc. Nat. Acad. Sci. 79:1979 (1982) for the statement that alteration of a single amino acid in the CDR of a myeloma protein resulted in loss of antigen-binding function. The Examiner concludes that undue experimentation would be required to produce the invention commensurate with the scope of the claims, citing *In re Fisher*, 166 U.S.P.Q. 18 (C.C.P.A. 1970).

Applicants respectively submit that the claims are enabled under the standards set forth in Wands. A specification is presumed to be enabling and the U.S. Patent and Trademark Office (PTO) has the burden of establishing a *prima facie* case of lack of enablement. See, In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976); In re Marzocchi, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). To make a *prima facie* case of lack of enablement, the PTO must come forward with reasons, supported by the record

as a whole, showing why the specification fails to enable one of ordinary skill in the art to make and use the claimed invention. In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). The mere fact that some experimentation is necessary does not negate enablement as long as undue experimentation is not required. See M.P.E.P. § 608.01(p).

The burden is on the PTO to establish that experimentation would be undue, Angstadt, 190 U.S.P.Q. at 219, taking into consideration the eight factors that are to be considered in determining whether a disclosure requires undue experimentation. In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Applicants submit that the amount of experimentation which may be required to practice the present invention does not rise to the level of being undue experimentation, as defined by the Court in Wands.

An important aspect of the Court's decision in Wands is its finding that the nature of the technology pertinent to the Wands invention (monoclonal antibody production) permitted a broad definition of the term "experiment." The Court found that an "experiment" in the monoclonal antibody art consisted of the entire attempt to make a monoclonal antibody against a particular antigen. As described by the Court, the process entailed, "immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics." 8 U.S.P.Q.2d at 1407. Thus, Wands supports the conclusion that in, a complex field such as monoclonal antibody production, the entire attempt to achieve the desired result, from beginning to end, constitutes one experiment.

According to the Court, repetition of this whole experiment more than once does not constitute undue experimentation. As the Court indicated, practitioners in the art would be prepared to screen negative hybridomas in order to find a hybridoma making the desired antibody. 8 U.S.P.Q.2d at 1406. Thus, the fact that some aspects of the experiment as a whole will yield negative results does not mandate a finding that the amount of experimentation to achieve a positive result is undue.

Like the production of monoclonal antibodies, the production of an antibody within the scope of claims 1 and 2 may require some experimentation, but if viewed in the light of Wands, this experimentation, and the possibility of encountering negative

results along the path to the positive results, is not undue. Furthermore, the present applicants provide extensive guidance to allow one of ordinary skill in the art to obtain a polypeptide that is within the scope of the claims.

Applicants submit that one of ordinary skill in the art can construct an antibody as described in the specification at least at page 36, lines 13-19, and in the sections of the specification cited below.

Applying this information to the eight Wands factors, one of skill in the art would conclude that undue experimentation would not be required to practice the claimed invention.

1. *Quantity of experimentation necessary.* To determine if an antibody falls within the scope of the claims, the only experimentation required is the performance of known antibody binding procedures. These procedures are routine and would not have to be done repeatedly before a definitive result was obtained. Because the inventors and the art provide means for the objective measurement of an antibody falling within the claim scope, this factor is met, for example, by the ability of a multimerized antibody to bind to CD83 polypeptide. This is described in the specification at least at page 39, lines 8-22; page 97, line 15 to page 101, line 22, particularly figures 27 and 28, and page 26, line 1 to page 27, line 2.

The Wands court found that practitioners in the art are prepared to screen negative hybridomas to find one that made the desired antibody. (USPQ2d at 1406.) The court further stated that an "experiment" was not simply the screening of a simple hybridoma, but instead was the entire attempt to make a monoclonal antibody against a particular antigen. This process included immunizing animals, fusing lymphocytes from the immunized animals to make hybridomas, cloning the hybridomas, and screen the antibodies produced by the hybridomas. (8 USPQ2d at 1406).

By analogy, a single experiment in the present art could include obtaining or constructing anti-CD83 antibodies, cross-linking them as described, and testing binding to a CD83 polypeptide. Encountering negative results would not mean that undue experimentation is involved, according to Wands.

2. *Amount of direction or guidance provided.* Examples 7 and 8 and the specification in general provide clear directions for performing the experimentation, and

the specification provides cites to published scientific articles for details not mentioned in the specification. Similarly, the Wands court found that the starting material was available to the public (as is the material used in the present application) and the patent at issue in Wands provided a detailed description of the methods, which included use of a commercially available kit. (8 USPQ 2d at 1404, 1405). The antibody used in applicants' methods is raised using materials available to the public, and the application describes the methods for multimerization, at pages 97-101.

3. *Presence of absence of working examples.* The specification describes production of multimerized antibodies to CD-83, specifically at pages 97, line 15 to page 101, line 22.

4. *Nature of the invention.* The invention relates to antibodies. Methods of raising antibodies are well-known in the art. This is indicated in the specification at, for example, page 32, line 27 to page 33, line 14. Thus, the nature of the invention is such that it is well-known to those of ordinary skill in the art. The court in Wands stated that the nature of monoclonal antibody technology is such that it involves screening, including screening of negative samples (in that case, hybridomas). The number of potentially negative samples was not viewed as a determining factor in reaching a finding of undue experimentation (8 USPQ 2d at 1406-1407). The application provides known methods of cross-linking antibodies, at, for example, page 26, line 1 to page 27, line 2.

5. *The state of the prior art.* The prior art provides the methods and materials needed to apply the methods of factor (4) above to anti-CD83 antibodies. The Wands court found that "all the methods needed to practice the invention were well-known." (8 USPQ 2d at 1406). Similarly, the methods of preparing an antibody, cross-linking, and measuring antigen binding to antibodies, are well known.

6. *The relative skill of those in the art.* Those of skill in this art are highly skilled and would be competent at designing and performing, or directing the performance of, the procedures of factors (4) and (5) above. The Wands court found that the level of skill in the monoclonal antibody art was high at the time the application was filed, but, importantly, the court found that development of skill in performing specific experiments relevant to the art did not preclude enablement. Specifically, the

court stated that initial failures occurred as the inventors learned to fuse cells, and "[o]nce they became skilled in the art, they invariably obtained numerous hybridomas ..." that met the claim limitations. (8 USPQ 2d at 1406). By analogy, it would not defeat enablement for one of skill in the art of antibody production and testing to learn and become proficient in techniques for practicing the present invention.

7. *The predictability or unpredictability of the art.* One of skill, being acquainted with the methods described in the application, would predict that when a polypeptide specifically binds to an antibody raised against CD83, multimerized anti-CD83 antibodies can also be tested for the ability to bind. This can be routinely confirmed by the methods of the Examples.

In Wands, the Court noted that the cell fusion technique was well known to those of ordinary skill in the art, and that there was no indication that the fusion step should be more difficult or unreliable for the antigen in question (HBsAg) than for other antigens. The present Examiner has provided no evidence that the multimerized anti-CD83 antibody binding steps would be "more difficult or unreliable" (8 USPQ2d at 1406) than for other antibodies.

8. *The breadth of the claims.* Using materials and methods routinely available at the time of filing, one of skill can identify or construct an antibody meeting the limitations of the claims, and test it for binding to a CD83 polypeptide antibody binding as described for the previous factors.

In view of the foregoing remarks, applicants submit that the Examiner has not met his burden of making a *prima facie* showing that undue experimentation is required in order to practice the invention as claimed. Reconsideration and withdrawal of this rejection are respectfully requested.

35 U.S.C. §102. Claims 1 and 2 are rejected under 35 U.S.C. §102(b) over WO 9729781 or U.S. Patent No. 5,766,570. According to the Examiner, WO '781 teaches an antibody that can bind to a CD83 polypeptide having a sequence 100% identical to SEQ ID NO:97 of the present application. U.S. '570 allegedly teaches an isolated antibody that can bind to HB 15, which is 100% % identical to SEQ ID NO:97. the Examiner stated that claim 2 is included in the rejection because the claimed functional

limitation allegedly would be an inherent property of the referenced antibody, since they bind to the same CD83 polypeptide.

Claims 1 and 2 have an important limitation in that the antibody is multimerized. The two cited references fail to disclose a multimerized antibody. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1 and 2 are rejected under 35 U.S.C. §102(e) over U.S. Patent No. 6,068,984. According to the Examiner, U.S. '984 teaches an antibody that can bind to a CD83 polypeptide having a sequence 100% identical to SEQ ID NO:97 of the present application. Claim 2 is included in the rejection because the claimed functional limitation allegedly would be an inherent property of the referenced antibody, since they bind to the same CD83 polypeptide.

As discussed above, claims 1 and 2 have the limitation that the antibody is multimerized. The cited reference fails to disclose a multimerized antibody. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-3 are rejected under 35 U.S.C. §102(e) over U.S. Patent Application No. 10/496,284. According to the Examiner, U.S. '284 teaches an antibody that comprises that same SEQ ID NOs:26, 28, 33, 37, 41, 45, 62, and 64 as claim 3. Claim 2 is included in the rejection because the claimed functional limitation allegedly would be an inherent property of the referenced antibody, since they bind to the same CD83 polypeptide.

In view of the claim 1 and 2 limitation that the antibody is multimerized, the cited reference fails to anticipate, because if does not disclose a multimerized antibody. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-3 are rejected on the ground of nonstatutory obviousness-type double patenting over claims 15-17 of co-pending U.S. Patent Application No. 10/496,284. A terminal disclaimer will be filed upon indication of allowable subject matter in either of the pending application.

If fees are believed necessary, the Commissioner is authorized to charge any required fee, deficiency or credit any overpayment to Deposit Account No. 04-0258. A duplicate copy of this document is enclosed.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
Leon Fernando Garcia-Martinez
DAVIS WRIGHT TREMAINE LLP

By _____
Jane E. R. Potter
Registration No. 33,332

2600 Century Square
1501 Fourth Avenue
Seattle, WA 98101-1688
Phone: (206) 622-3150
Facsimile: (206) 628-7699